

IN THE CLAIMS:

1. (Currently amended) A method for detecting a variant HBV which exhibits an altered sensitivity to an agent, said method comprising:

generating a genetic construct comprising a replication competent amount of the genome from said variant HBV contained in or fused to an amount of a baculovirus genome capable to infect ~~of infecting hepatocyte cells of hepatic origin~~ and then infecting said cells with said construct;

contacting said cells, before, during, or after infection, with the agent to be tested;

optionally further infecting said cells with the same genetic construct or a genetic construct comprising the genome of HBV wild type or another HBV variant;

culturing said cells for a time and under conditions sufficient for the variant HBV to be detected to replicate, express genetic sequences or assemble or release virus or virus-like particles if resistant to said agent; and

subjecting the cells, cell lysates or culture supernatant fluid to viral- or viral-component-detection means to determine whether or not the variant HBV has replicated, expressed genetic material, assembled, or been released in the presence of said agent.

2. (Original) A method according to Claim 1 wherein the variant HBV is capable of replicating in the presence of an agent which inhibits or reduces infection, replication or assembly of a reference HBV.

3. (Original) A method according to Claim 2 wherein the agent is a nucleoside analogue or a non-nucleoside analogue.

4. (Previously presented) A method according to Claim 3 wherein the agent is a non-nucleoside analogue reverse transcriptase inhibitor, a non-nucleoside analogue DNA dependent DNA polymerase inhibitor, or both a non-nucleoside analogue reverse transcriptase inhibitor and a non-nucleoside analogue DNA dependent DNA polymerase inhibitor.

5. (Original) A method according to Claim 3 wherein the nucleoside analogue is 3TC, PMEA or PCV.

6. (Original) A method according to Claim 2 wherein the agent is an immunointeractive molecule.

7. (Original) A method according to Claim 6 wherein the immunointeractive molecule is an antibody.

8. (Previously presented) A method according to any one of Claims 1 to 7 wherein the variant HBV comprises an altered HBV DNA polymerase, an altered HBV precore promoter or basal core promoter, an altered HBsAg, or a combination thereof.

9. (Currently amended) A method according to Claim 8 wherein the altered ~~HB~~HBV DNA polymerase is selected from the group consisting of L426I/V, L428I/VN480G, N485K, K495R, R499Q, G499E, W499Q, F512L, I515L, V519L, L526M, M550V, M550I, V553I, S565P.

10. (Previously presented) A method according to any one of Claim 1 to 8 wherein the variant HBV is a multiple mutant selected from the group consisting of L526M/M550I, L526M/M550V, V519L/L526M/M550V and V519L/L526M/M550I.

11. (Canceled)

12. (Previously presented) A method according to Claim 8 wherein the altered HBV precore promoter or basal core promoter is selected from the group consisting of A1814T, C1856T, G1896A, G1897A, G1898A, G1899A, G1896A/ G1899A, A1762T/G1764A, T1753C, G1757A and C1653T (where the numbering is from the unique *Eco*R1 site in HBV).

13. (Canceled)

14. (Previously presented) A method according to Claim 8 wherein the altered HBsAg is selected from the group consisting of G112R, T123P Y/F134S, D144E, G145R, A157D, E164D, F170L, M195I, W196L, W196S, W196STOP, M198I, W199S, S204T, S210R.

15. (Previously presented) A method according to Claim 8 wherein the altered HBsAg is selected from the group consisting of D144E, G145R, A157D, E164D, M195I, W196L, W196L, W196S, W196STOP, M198I, W199S and S210R.

16-20. (Canceled)

21. (Currently amended) A method according to Claim 8 wherein the cells are co-infected with multiple combinations of the different variant HBVs ~~comprises~~ comprising an altered HBV precore promoter or basal core promoter or an altered HBV HBsAg or an altered HBV DNA polymerase or combinations thereof.

22. (Currently amended) A method according to Claim 8 wherein the cells are superinfected with multiple combinations of the different variant HBVs comprising an altered HBV precore promoter or basal core promoter or an altered HBV HBsAg or an altered HBV DNA polymerase or combinations thereof.

23. (Currently amended) A method for detecting a variant HBV comprising DNA polymerase which exhibits an altered sensitivity to an agent, said method comprising:

generating a genetic construct comprising a replication competent amount of the genome from said variant HBV contained in or fused to an amount of a baculovirus genome capable to ~~infect~~ of infecting hepatocyte cells of hepatic origin and then infecting said cells with said construct;

contacting said cells, before, during, or after infection, with the agent to be tested;

optionally further infecting said cells with the same genetic construct or a genetic construct comprising the genome of HBV wild type or another HBV variant;

culturing said cells for a time and under conditions sufficient for the variant HBV to be detected to replicate, express genetic sequences, assemble, or release virus or virus-like particles if resistant to said agent; and

subjecting the cells, cell lysates or culture supernatant fluid or virus purified therefrom to HBV DNA polymerase assay in the presence or absence of said agent to determine whether said variant HBV exhibits an altered sensitivity to said agent, wherein said agent comprises nucleoside triphosphate analogues or non-nucleoside analogue reverse transcriptase inhibitors or non-nucleoside analogue DNA dependent DNA polymerase inhibitors.

24. (Currently amended) A method for detecting HBV DNA polymerase activity in the presence of an antiviral agent said method comprising:

generating a genetic construct comprising a replication competent amount of a genome from an HBV capable of producing said DNA polymerase, said genome contained in or fused to an amount of a baculovirus genome capable to ~~infect~~ of infecting hepatocyte cells of hepatic origin and then infecting said cells with said construct;

contacting said cells, before, during, or after infection, with the agent to be tested;

optionally further infecting said cells with the same genetic construct or a genetic construct comprising the genome of HBV wild type or another HBV strain;

culturing said cells for a time and under conditions sufficient for ~~the~~ said variant HBV to replicate, express genetic sequences, assemble, or release virus or virus-like particles if resistant to said agent; and

subjecting the cells, cell lysates or culture supernatant fluid or virus purified therefrom to an HBV DNA polymerase assay in the presence or absence of said antiviral agent to determine whether said variant HBV exhibits an altered sensitivity to said antiviral agent, wherein said antiviral agent comprises nucleoside triphosphate analogues or non-nucleoside analogue reverse transcriptase inhibitors or non-nucleoside analogue DNA dependent DNA polymerase inhibitors.